between quality indicators and hard outcomes were tested using Cox regression adjusting for confounding, reporting hazard ratios (HR) with 95% confidence intervals.
Results: Lipid and albuminuria-lowering treatment status were associated with a lower risk of the composite outcome (HR = 0.77 [0.67, 0.88]; HR = 0.75 [0.59, 0.94]). Glucose-lowering treatment status was associated with a lower risk of the composite outcome only in patients with an elevated HbA1c level (HR = 0.72 [0.56, 0.93]). Blood pressure–lowering treatment status was not associated with a risk of the composite outcome. Treatment intensification with glucose lowering but not with lipid-, blood pressure–, and albuminuria-lowering drugs was also associated with a lower risk of the composite outcome (HR = 0.73 [0.60, 0.89]).
Conclusion: Treatment quality indicators measuring lipid- and albuminuria-lowering treatment status are valid quality measures because they predict a lower risk of cardiovascular events and mortality in patients with diabetes. The quality indicator measuring glucose-lowering treatment status should only be used for restricted populations with elevated HbA1c levels. Intriguingly, the tested indicators measuring blood pressure–lowering treatment status and treatment intensification with lipid-, blood pressure–, and albuminuria-lowering drugs did not predict patient outcomes. These results question whether all of the currently used and proposed treatment indicators are valid to judge health care and economics.
Disclosure of Interest: None declared.

OC024—ADDRESSING THE CHALLENGES OF DIABETES AND ITS COMPLICATION: THE IMI DIABETES PLATFORM

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Introduction: The identification of novel genes or cellular pathways that are involved in pancreatic β-cell function, and the development of reliable probes for the in vivo imaging of β cells are key challenges of the current diabetes treatment. Furthermore, the discovery and the validation of biomarkers that are predictive for the progression of glycemic deterioration and treatment response to current standard therapies or for the development of diabetic macro- and microvascular complications will lead to more effective and safer treatment of diabetes by patient stratification in a personalized medicines approach of their treatment.
Patients (or Materials) and Methods: The 3 diabetes projects of the Innovative Medicines Initiative (IMI)—IMIDIA, SUMMIT, and DIRECT—are focusing on different stages of diabetes development. While the focus of IMIDIA is the function of the pancreatic β cell and its in vivo imaging, the key aspects of DIRECT and SUMMIT are the identification and validation of biomarkers predictive for progression of diabetes and treatment response, and for the development of late stage complications during disease progression. These 3 consortia form the IMI Diabetes Platform.
Results: In IMIDIA, launched on February 1, 2010, twelve academic institutions, 8 Pharma partners, and 1 small and medium-sized enterprise (SME) are working together to elucidate novel pathways that improve β-cell function and to identify diagnostic biomarkers for treatment monitoring in diabetes. The 5-year project addresses key bottlenecks in the development of β-cell–focused therapies. The DIRECT consortium consisting of 21 academic institutions and 4 Pharma partners addresses the personalized medicines approach in type 2 diabetes patients. The focus of the consortium is the identification of surrogate markers that can be used for patient stratification according to glycemic deterioration of patients at high risk for diabetes or early onset of diabetes and makers predictive for response to current standard therapies of type 2 diabetes. DIRECT was launched on February 1, 2012. In SUMMIT, the joint research of 19 academic institutions, 6 Pharma partners, and 1 SME addresses the urgent need for novel treatments of diabetic complications beyond glucose-lowering therapies. The key aspect of the consortium is the identification and validation of surrogate markers for the development of micro- and macrovascular complications during progression of diabetes. The project was launched on November 1, 2009.
Conclusion: Each single participant cannot undertake this holistic approach of the IMI Diabetes Platform alone. The close collaboration between expert institutes for diabetes research and clinical development is required to achieve the ambitious goals of the diabetes consortia.
Disclosure of Interest: None declared.

OC025—REVERSAL STRATEGY IN ANTAGONIZING THE P2Y12-INHIBITOR TICAGRELOR

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Introduction: Patients on antiplatelet therapy have a higher incidence of bleeding complications and reversal of antiplatelet drug effects is an important issue at trauma or emergency departments. For old and conventional anticoagulants, reversal strategies are established. However, there is no experience or recommendation how to antagonize the reversible and highly effective P2Y12-inhibitor ticagrelor and how to restore platelet function after ticagrelor dosing. The aim of the study was to describe an ex vivo model to reverse the effects of ticagrelor and to estimate the optimal quantity of platelet transfusions required to normalize platelet aggregation.
Patients (or Materials) and Methods: To normalize platelet aggregation, increasing amounts of autologous platelet-rich plasma (PRP) were added ex vivo to hirudin-anticoagulated blood which was obtained 3 hours after the administration of ticagrelor, by spiking PRP into blood at ratios of 1:10, 1:5, and 1:3. Platelet aggregation was assessed by whole blood multiple electrode aggregometry (MEA; Multiplate®). For interpretation of aggregation, we defined a cutoff level of 40 A.U. as the lower limit of the range. Volunteers above this level were considered to exhibit normal platelet reactivity. Nonparametric tests were used and statistical comparisons were performed with the Friedman ANOVA, and the Wilcoxon test for post hoc comparisons. A 2-tailed P value <0.05 was considered significant.
Results: The strategy to reverse the effect of ticagrelor was tested in 20 healthy volunteers. A clear dose-response was obtained after spiking whole blood with increasing amounts of PRP. After addition of PRP at a ratio of 1:10, platelet aggregation increased to 31 ± 14 A.U. When assuming that 1 apheresis platelet concentrate (200 mL) typically contains a minimum of 2×1011 platelets, the ratio of 1:10 corresponds to 0.5 unit of apheresis platelet concentrates. A ratio of 1:5—equivalent to 1 unit of platelet concentrates—increased ADP induced platelet aggregation to 41 ± 14 A.U. Platelet aggregation increased further to 48 ± 18 A.U. following the addition of PRP at a ratio of 1:3, which corresponds to 1.5 units of platelet concentrates. All comparisons were significant at $P < 0.01$.
Conclusion: Platelets dose-dependently improve ex vivo platelet aggregation of subjects after a loading dose of 180 mg of ticagrelor. It is estimated that >2 units of apheresis platelet concentrates will be necessary to completely restore baseline platelet aggregation in the majority of patients. Point-of-care platelet function tests may be suitable tools to verify this concept in emergency patients and to estimate the extent of the reversal and de-risk on an individual patient's level.
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